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EXAMINER
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09/25/89 2163

Resp 12-25-89
Resp Next 3-25-90

SEP 28 1989

DHH/LHP HOPK

☒ This application has been examined ☐ Responsive to communication filed on Sept 9, 89 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-22, 27-30 are pending in the application.
   Of the above, claims 11-22, 27-30 are withdrawn from consideration.
2. ☒ Claims 23-26 have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-10 are rejected.
5. ☒ Claims 1-10 are objected to.
6. ☒ Claims 1-22, 27-30 are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

I. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-10, drawn to a hybridoma and the monoclonal antibody that it produces, classified in Class 435, subclass 240.27 and class 530, subclass 387.

II. Claims 11-22, drawn to a method of producing purified stem cells, classified in Class 435, subclass 240.21.

III. Claims 27-30, drawn to a method of medical treatment classified in Class 424, subclass 95.

A. Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP 806.05(h)). In the instant case the method of Group II may be practiced with a product such as polyclonal antibodies or a hybridoma antibody recognizing a different epitope on the same antigen. the hybridoma antibody of Group I can be used in a different process, such as a diagnostic assay.

B. The process of Group III represents a method of using the product which would result from the method of Group II. These methods are independent and distinct from each other. Further, the method of Group III does not require the products of Group I.

C. During a telephone conversation with Sarah Kegan on March 22, 1989 as authorized by Dale H. Hoscheit, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-10.

Affirmation of this election must be made by applicant in responding to this Office action. Claims 11-22 and 27-30 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 23-26 have been canceled by applicant in Paper 2, entered June 1, 1987.

II. The specification and claims should be checked for errors. Examples of such errors follow:

1. In the abstract: "theraputic" for "therapeutic".

2. page 2, 3rd ¶: "anethesia" for "anesthesia".

3. page 14, line 10: "insotypes" for "isotypes".

III. The specification should contain:

Updating of the status of all related applications referred to in the specification is required *ie:* "This application is a division of 06/670,740 filed 02/06/84 (allowed). Now U.S. patent 4,714,680, issued 12/22/87.

IV. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

A. The specification is objected to under 35 U.S.C. 112, first paragraph, as failing to provide an adequate written description of the invention, failing to provide an enabling disclosure and failing to present the best mode contemplated by applicant for carrying out the invention without complete evidence of the deposit of the anti-My-10 monoclonal antibody used in the experiments described within the specification. It is unclear

whether the anti-My-10 monoclonal antibodies of the specification are identical to the monoclonal antibody of ATCC Accession No. HB-8483. Is a single monoclonal antibody used for all the anti-My-10 experiments in the specification, or is there described a family of anti-My-10 monoclonal antibodies that may have different isotypes, affinities, or antigen combining sites? It is unclear whether the specific hybridomas claimed could be reproduced without undue experimentation. Further, the broader claims such as claims 1 and 2 require the deposit of the KG-1a cell line to be enabling.

The specification lacks complete deposit information for the deposit of relevant anti-My-10 producing hybridomas, ATCC Acc. No. HB-8483, and the cell line, KG-1a, to which monoclonal antibodies were made. It does not appear that the anti-My-10 producing hybridomas can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the hybridomas producing these monoclonal antibodies and also the KG-1a cell line to which the monoclonal antibodies were produced. The deposit of the anti-My-10 producing hybridomas and also the KG-1a cell line is required. No statement has been made on the record that the relevant anti-My-10 producing hybridomas or that the KG-1a cell line are available to the public, nor that they may be reproducibly derived.

Applicant's referral to deposit of HB-8483 at page 3 of the specification is an insufficient assurance that all required deposits have been made and the conditions of M.P.E.P. 608.01(p)(C) met.

B. If the deposits were made under the provisions of the Budapest Treaty, 1) filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that (a) the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, and that (b) all restrictions upon public access to the deposits will be

irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. 2) Amendment of the specification to recite the date of the deposit and the complete name and address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

C. If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in M.P.E.P. 608.01(p)(C), items 1-3 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has authority and control over the conditions of deposit, over his or her signature and registration number, averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon availability of the deposits to the public will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of thirty years from the date of deposit or for the enforceable life of a patent or for a period of five years after the date of the most recent request for a sample of the deposits, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the complete name and address of the depository is required. As a possible means for completing

the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposits were made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the anti-My-10 producing hybridomas used in all the experiments of the specification and that the KG-1a cell line have been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposits will be irrevocably removed upon the grant of a patent on this application is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the complete name and address of the depository is required. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit. Applicant's attention is directed to In re Lundak, 773 F.2d 1216, 227 U.S.P.Q. 90 (CAFC 1985) and M.P.E.P. 608.01(p)(C) for further guidance. V. Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification.

VI. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to the hybridomas and associated anti-My-10 antibodies used to generate the data of the disclosure. See MPEP 706.03(n) and 706.03(z).

VII. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2 are indefinite and vague in their recitation of the term "normal". Does this term refer to cells isolated from either cell culture or freshly from patients? Does it refer to cells from humans without cancer or other blood disorders such as Epstein Barr Virus infection? Is a sickle-cell stem cell "normal"? It is suggested that a phrase such as "cells from humans without hematopoietic disorders or diseases" would more specifically define the claim.

VIII. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action :

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

IX. Claims rejected under 35 U.S.C. 102(a) as being anticipated by AR2 (Civin, 1983), AS2 (Civin, 1983), AT2 (Civin, 1983), and AR3 (Strauss, 1983). These four abstracts all teach the MY-10 antigen, the monoclonal antibody that identifies it and the use of such monoclonal antibodies in the characterization of hematopoietic cells.

X. Claims rejected under 35 U.S.C. 102(b) as being anticipated by AS (Civin, 1982) and AT (Civin, 1982). These two abstracts teach the MY-10

antigen, monoclonal antibodies identifying it and use of these monoclonal antibodies in differentiating hematopoietic cells.

XI. The following is a quotation of 35 U.S.C. 103 which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

XII. Claims 1-10 are rejected under 35 U.S.C. 102(a) or (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over AR4 (Bodger, May 1983), AS4 (Bodger, 1981) and AT4 (Nadler, 1981). These references describe monoclonal antibodies to epitopes of human hematopoietic precursor cells. *Prima facie* it appears that the monoclonals taught by the Bodger references and by Nadler, pages 212-215 may be the same as those of the instant claims. It is unclear whether these monoclonal

antibodies have been compared to each other under similar conditions. The burden of proof is shifted to the applicant to show that the same *epitopes* are not recognized by the Bodger monoclonals and those of the instant claims.

XIII. Claims 1-10 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over A (Dupont 4,710,457), C (Kung 4,624,925), D (Kung 4,364,932), E (Kung 4,364,937), or AB (Kung 4,381,295), B (Trowbridge 4,582,797). According to AR (Civin, 1984), p.162:

> **'The expression of MY-10 on a variety of nonmyeloid cell types (including the many malignant and minor lymphoid cell sub-types) remains to be determined."**

Prima facie it appears that the MY-10 antigen was defined only in relation to cell surfaces. If other hematopoietic cells have non-surface-exposed MY-10 antigen, then other monoclonal antibodies, such as those taught by the references above, may recognize MY-10 on the basis of other screening techniques such as Western-blotting or ELISA testing of disrupted hematopoietic cells. The references above describe isolation of hybridomas producing monoclonal antibodies which react with particular types of hematopoietic cells. No evidence is presented that the same antigens or epitopes recognized by these monoclonal antibodies are not the same as those recognized by the monoclonal antibodies of the instant claims.

XIV. Claims 1-10 are rejected under 35 U.S.C. 103 as being unpatentable over Nadler in view of the known availability of leukemic cell lines like KG-1 or KG-1a (AS, AT, AR2, and the specification page 5). Nadler (p.188) teaches:

> **. . .the production and characterization of monoclonal antibodies; . . .the characterization of subpopulations of immune cells expressing unique antigens; . . .leukemias and lymphomas utilizing both lineage and differentiation associated antigens; and . . .the clinical, diagnostic and therapeutic utility of these antibodies.**

Nadler teaches monoclonal antibodies to particular hematopoietic cell lines and also the rationale for developing such monoclonals. Nadler does not teach the particular cell line used in the specification. The Civin references and the specification teach the particular relevance of the hematopoietic cell line used to make the products of the instant claims. It would have been obvious to one with ordinary skill in the art to use the techniques and rationale of Nadler to make the claimed hybridomas and monoclonal antibodies from the known KG-1a cell line for the purposes set forth by Nadler.

XV. Reference F (Civin) is cited as a reference of interest to complete the record only.

XVI. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Thomas M. Cunningham, Ph.D whose telephone number is (703) 557-8871. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 557-3920.

MARGARET MOSKOWITZ
SUPERVISORY
PATENT EXAMINER
ART UNIT 186

Cunningham

9/21/89